A Tale of Birds, pigs and men ….

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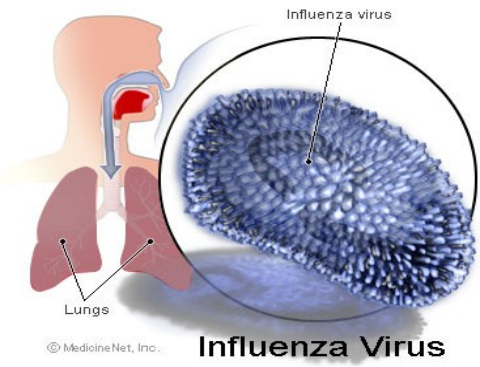
Force Health Protection and Readiness

Agenda

- Seasonal Influenza
  - Impact
  - Prevention
- Pandemic Influenza
  - Clinical features
  - DoD Plans/Guidance
  - Vaccine
  - Antivirals
  - Antibiotics
  - PPE
  - Communication

Influenza Virus



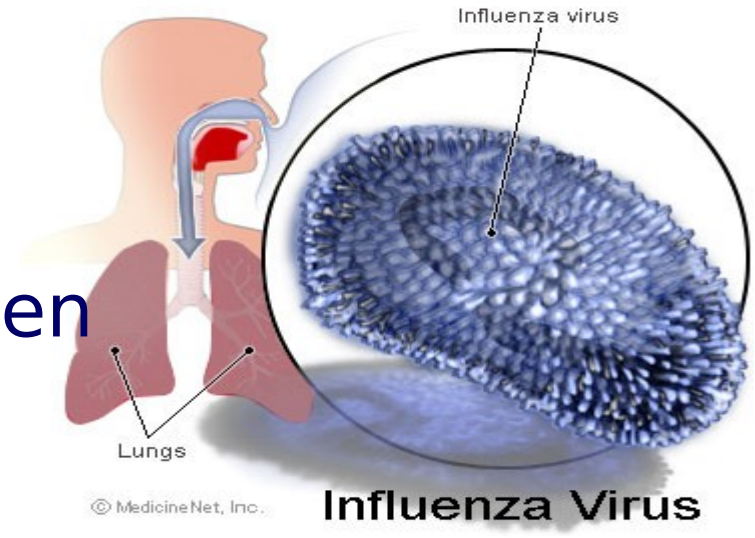
- **Influenza is a contagious respiratory disease caused by influenza type A or influenza type B viruses**
- **Influenza viruses continuously change, requiring production of a new influenza vaccine each year**
- **Vaccines against one influenza virus provides limited or no protection against another type or subtype of influenza**
- **Scientists correctly predict what type A influenza virus strains will circulate during the next influenza season 9 times out of 10 and about 50% of the time for type B**

Influenza

- Virus structure
  - ss RNA
  - No proof reading - high degree of mutation
    - Drift (small changes) or shift (significant change)
      - 1918 pandemic - shift from avian derived virus
  - 8 gene segments coding 10 proteins
    - Simultaneous infections result in potential REASSORTMENT of the 16 viral segments into new strain
      - Last three pandemics
  - Viral coating - more intact and tenacious during colder months (flu goo)

Strain Nomenclature

- H = hemagglutinin antigen type – lung Velcro



- N = neuraminidase enzyme type – Elvis has left the building

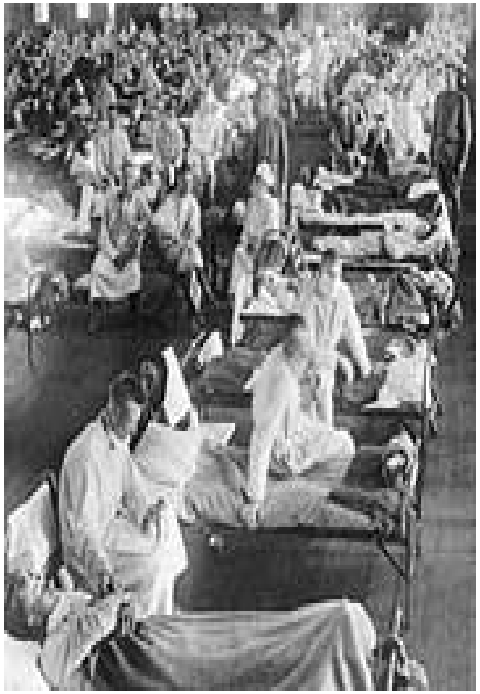
How is Influenza Spread

- Influenza virus is spread by airborne respiratory droplets aerosolized during coughing or sneezing
- Direct contact with droplets accounts for about 80% of all infections

- 20% of influenza infections are from touching surfaces that have been contaminated with aerosolized droplets then touching your eyes, mouth, or nose

A & B Type Influenza

- Influenza seasons in which influenza A viruses predominate are associated with higher mortality and more hospitalizations
- Mid 70’s to 1990 type A flu predominated about half the time
- Influenza A viruses have been the predominant type since the early 1990’s



Why be so concerned about the flu?

- Typically influenza kills 35,000 Americans each year
- Attacks children and the elderly with those over 65 years of age accounting for >90% of influenza deaths
- Although people with pre-existing medical conditions are at highest risk of severe complications following an influenza infection, each year healthy young adults and children become severely ill and die

Seasonal Influenza Impact

- Influenza secondary effects
  - In hospitals without mandatory immunization of health care providers all cause mortality and hospital length of stays increase sharply during the flu season.
  - Influenza is responsible for increases in heart attacks and stroke
    - When patients are protected rates dramatically decrease
    - Flu causes up to 420,000 excess hospital admissions

Influenza Symptoms

- Symptoms include: fever, muscle aches, headache, malaise, nonproductive cough, sore throat, and runny nose
- Usually last about 7 days although some symptoms can persist for weeks-months
- Influenza infection can lead to more serious conditions such as pneumonia & heart disease
- Influenza infection can cause high fever leading to febrile seizures in children

- It’s not just the flu. Influenza can kill you!

Best protection against seasonal flu

- Immunization is the key to prevention
- Two types of flu vaccine are available
  - Nasal, Live Attenuated Influenza Vaccine (LAIV)
  - Injectable, Inactivated Influenza Vaccine (TIV)
- DoD purchases about 3M doses of influenza vaccine each year

Seasonal Influenza

- 1940s - first seasonal influenza vaccine was developed by the Department of Defense
  - Method remains largely unchanged
  - Start of DoD requirement for universal immunization of active duty members
- DoD conducts a mass immunization program yearly
  - We begin immunizing active duty members in Aug-September and achieve over 90% immunization rates by December

Which vaccine is best

- Depends on who is getting it
- LAIV clearly better for children and new recruits/accessions
- TIV may be slightly better for older service members
- DoD policy is to use LAIV for all new accessions and anyone else in whom LAIV is not contraindicated for medical or operational reasons

Production to Policy

- Manufacturer develops “best guess” strain production
- CDC, DoD presents strain and seed data to FDA’s vaccines and related biological products advisory committee (VRBPAC) who then determine composition of that seasons influenza vaccine composition (H3N2, H1N1, B)
- Manufacturer then produces vaccine
  - 3 strain changes for this year (first time in 30 years)
- ACIP (Advisory Committee on Immunization Practices) determines use guidelines
  - Expanded recommendations to pediatric population
- DoD releases seasonal flu policy
  - Services release service specific policy based on DoD policy
  - DoD typically purchases 3.5M doses (>1M LAIV)

DoD Flu Policy

- Mandatory immunization for all active duty
- Mandatory immunization for all those providing direct patient care
- Thimerosal – try to adhere to state statutes but don't withhold vaccine
  - If you are worried about mercury don't eat tuna but still get immunized

Pandemic Flu

Old Question: Will I get bird flu from touching a chicken?

H5N1 ------ It's still here

- Depends on what you do with chickens
- July 1: New human case in Egypt
  - Of 81 cases in Egypt, 27 have been fatal
- 436 cases with 262 deaths since 2003
- 41 cases with 12 deaths in 2009
    - 7 in China, with 4 deaths
    - 30 in Egypt, with 4 deaths
    - 4 in Vietnam, with 4 deaths

H5N1 transmission

- Most cases linked with close intimate contact with dead or sick fowl
- Limited human-to-human transmission
  - Primarily in blood relatives
  - One case of transmission to a healthcare worker
- Unique pathology with fulminant viral pneumonia and cytokine storm
- Major limiting factor for the virus is a primary attachment site deep in lung rather than in the upper airway

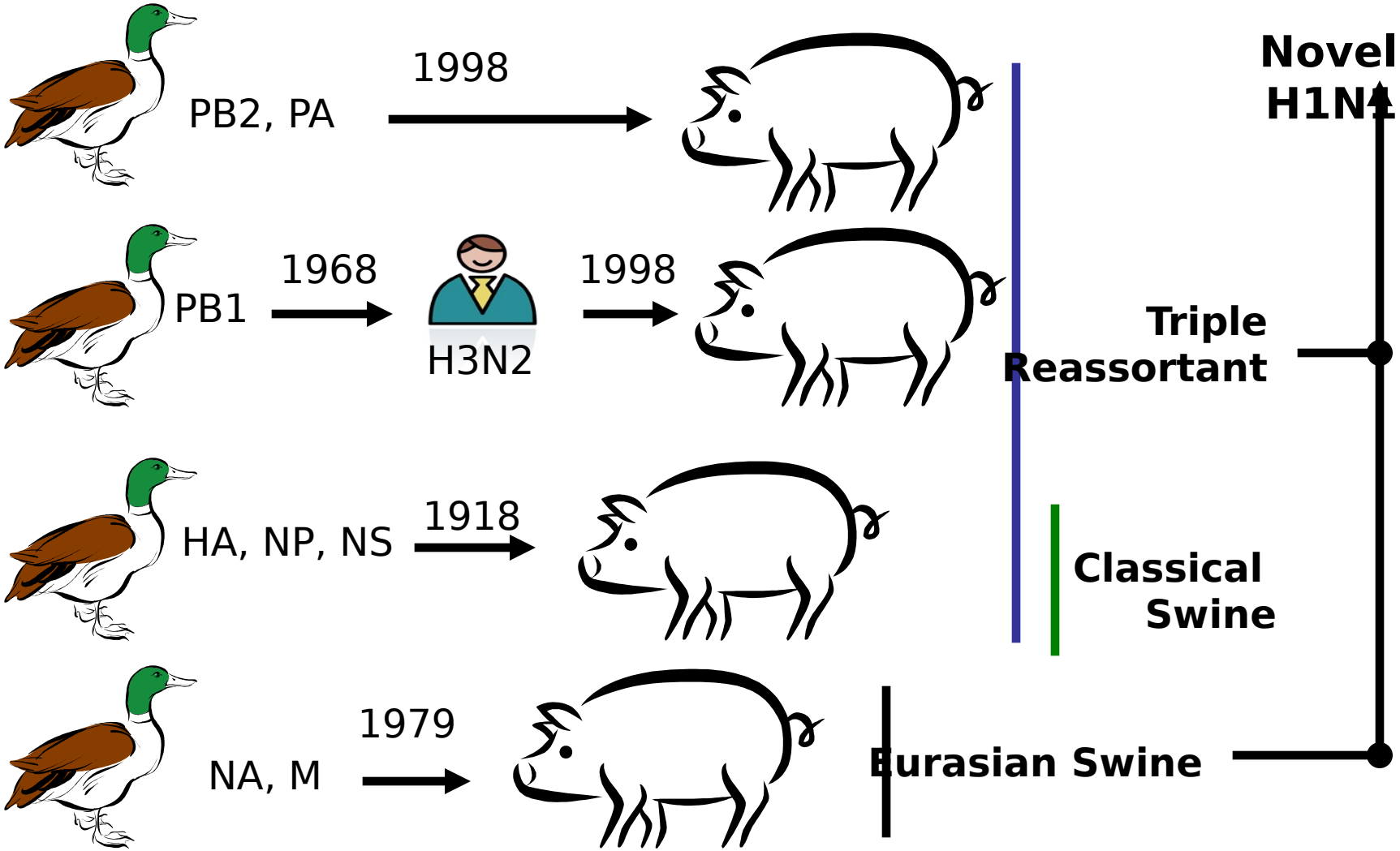
New question: Will I get swine flu from touching or eating pigs?

OWEN HUMPHRIES/PA/EPA

Novel Influenza A (H1N1)

- No matter what you do with pigs, you catch Novel H1N1 from people
- April 15 & 17: A novel swine origin influenza A (H1N1) virus was identified from two unlinked patients in the US
- At the same time widespread ILI was noted in Mexico
- Disease then spread across the US and internationally
  - Initially linked with travel to Mexico
- DoD surveillance assets identified the first four cases in the US - two cases each in California and Texas.
  - Out of the first 8 cases in the US, DoD identified 5.

Origins for the gene segments of the 2009 A(H1N1) virus



Novel H1N1 – International

- May have started in Jan 09 - Mexico
  - Case Fatality Rate 0.4% (0.3-1.5%) - Mexico
  - Clinical severity less than 1918, comparable to 1957
  - Attack rates <15 years of age 61%, ≥15 29%
  - Ro estimates 1.4-1.6 c/w 14 to 73 generations of human-to-human transmission
- International: 70,893 cases in 117 countries
  - All deaths except 2 are in the Americas

rguson et al. Science DOI: 10.1126/science.1176062***Science Express Index*****Reports**

Novel H1N1 – US Epidemiology

- Secondary attack rate in household contacts:
  - ARI – 19%
  - ILI – 12%
- 51% male
- Age: Median age 12, range 3 months to 81 years but median age for hospitalization is 20.
  - 18% between 0 & 4 years old
  - 41% between 5 & 24 years old
  - 34% between 25 and 64 years old
  - 4% equal to or over 65 years old

Novel H1N1 – US Epidemiology

- **Number of confirmed cases 37,246, Deaths 211, Hospitalizations 4,132**
- **Current estimate is > 1,000,000 cases in the US**
- **Hospitalizations 7.8%**
  - **71% with an underlying condition**
  - **18% with respiratory failure**
  - **21% ICU admission**
  - **41% with pre-existing medical condition**
  - **16% with prior flu vaccination**
- **Case fatality rate 0.2%**

Clinical Symptoms

- Clinical Symptoms (Hospitalized pts)
  - Fever 94% (92%)
  - Cough 92% (84%)
  - Sore throat 66% (30%)
  - GI symptoms 38%
  - Shortness of breath (54%)

Novel H1N1 – Who Dies?

- Current strains cause mild disease for most
- US deaths
  - >70% with underlying health conditions
  - More people under the age of 65 are hospitalized but more people who are over 65 and are hospitalized die.

Novel H1N1 – Primary Concern

- Virus has gone south for the winter
- Further mutation via genetic shift, drift or reassortant leading to bad vaccine match and/or increased antiviral resistance
- May result in a more virulent virus surfacing during the next flu season in the northern hemisphere
- May start before flu season

Mitigation Measures

Antivirals

- Oseltamivir represents the primary antiviral drug in the DoD stockpile
- Two stockpiles (tactical and strategic):
  - More than 8 million treatment courses
  - OCONUS COCOMS equivalent to 30% of PAR
  - CONUS MTFs equivalent to 30% of PAR
  - Three strategic depots: Approximately 7 million treatment courses
- Have requested funding for addition of Zanamivir

DoD Antiviral Strategy – H1N1

- Treatment for people hospitalized with confirmed, probable or suspected disease
- If suspected disease, treat if at high risk of influenza complications
- Consider post-exposure prophylaxis if at high risk for complications or if operational considerations mandate
- Treatment not necessarily indicated if healthy with mild confirmed disease
- VERY limited outbreak prophylaxis

H5N1 Antiviral Strategy

- Early treatment to reduce viral load
  - Disease exacerbation and death are associated with increased viral replication
  - Delay in therapy may be irreparable
- Post-exposure prophylaxis for known household contacts
- Limited outbreak prophylaxis

It all a matter of paying attention

Vaccines

- H5N1
  - Both HHS and DoD maintain a stockpile of pre-pandemic vaccines
  - Unadjuvanted vaccine provides limited protection
  - Addition of vaccine adjuvants will likely increase effectiveness and decrease required dose
- H1N1
  - Vaccine expected to be ready to be ready in September/October if not adjuvanted – November/December if adjuvanted
  - Unknown if H1N1 vaccine will be adjuvanted

Vaccine Prime-Boost Strategies

- For any novel influenza vaccine – need 2 doses about 28 days apart
- H5N1
  - Using a pre-pandemic vaccine as an immune system primer may need only one dose of the pandemic specific vaccine
- H1N1
  - Unknown if seasonal influenza vaccine can be used as a primer for novel H1N1 specific vaccine

Adjuvants

- Most effective adjuvants are an oil and water emulsion
- Boost the effect of vaccine
- Alone – no effect
- Better cross protection
- Lower dose
- More pronounced immune effect

Adjuvants

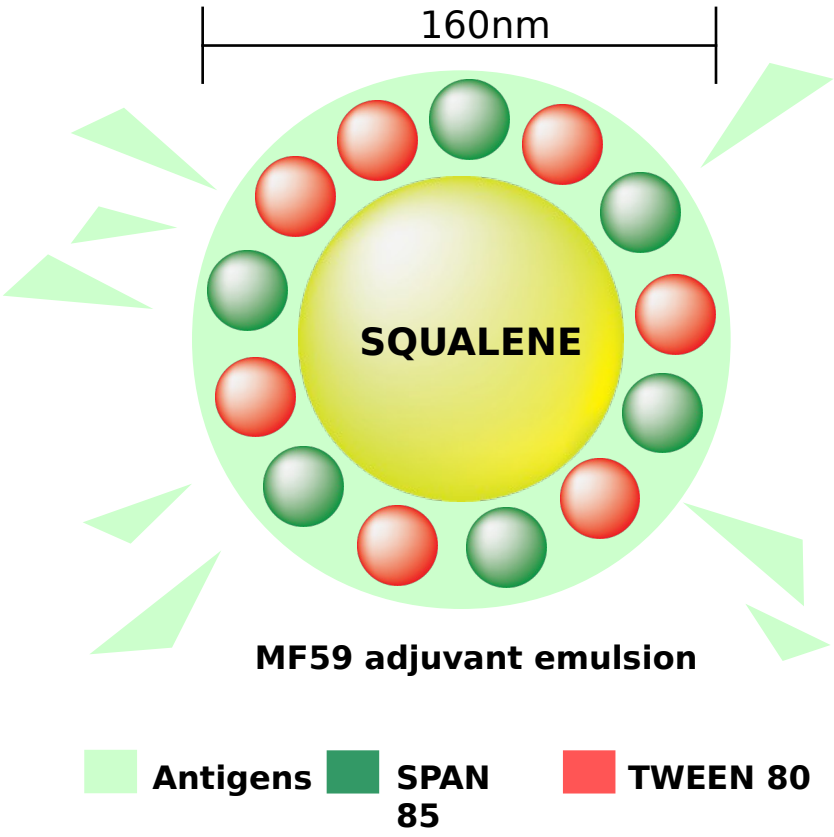
- Alum
  - Modest dose sparing
  - Batch-to-batch variation
  - Possible hypersensitivity reaction
- MF59
  - Dose sparing
  - Boostable
  - Cross protection
- AS-03
  - Dose sparing
  - Boostable
  - Cross protection
  - Three log decrease in lung viral titers with 3.8ug dose

MF59

Established Safety and tolerability

Boostable immunity and flexible dosing

- Oil-in-water adjuvant used in a licensed influenza vaccine
- More than 10 years of clinical and commercial experience
- Licensed for use in seasonal influenza vaccine FLUAD in the EU since 1997
- More than 40 million commercial doses distributed
- Studied in more than 26,000 subjects, including children



Novartis Vaccines, pharmacovigilance data on file; Podda A, Del Giudice G. *Exp Rev Vaccines* 2003;2:197−204; O'Hagan. *Exp Rev Vaccines* 2007; 6:699−710.

Adjuvants

- CDC engaged in mix-and-match study
  - Different adjuvants with different vaccines
  - Hopefully will answer the question:
    - Can you use one manufacturer's vaccine and another adjuvant and get the same effect?
    - Animal data suggests this is a viable option
    - Human trials have begun

H1N1 vaccine – Manufacturers and Proportion of US Supply

- Vaccines
  - CSL 18.7%
  - Sanofi Pastuer 26.4%
  - GSK 3.4%
  - Novartis 45.7%
  - MedImmune 5.8%
- Adjuvants
  - Novartis (MF 59) & GSK (AS 03)

Will novel H1N1 vaccine be adjuvanted?

- Depends on:
  - Disease severity increases
  - Vaccine production yields are very low
  - Virus mutates so much that the vaccine is a poor match
  - Transmission rates are higher than expected

When will novel H1N1 vaccine be available?

- It depends:
  - If all goes well non-adjuvanted vaccine may be available in September
  - If an adjuvanted vaccine is required FDA not likely to approve until October but probably Nov-Dec
  - May see a hybrid with non-adjuvanted vaccine released first followed by adjuvanted vaccine
  - DoD preference most likely adjuvanted vaccine

H1N1 vaccine – Where does DoD fit in?

- Pilot lots now being produced by the manufacturers
- Clinical data will be obtained after completion of pilot lots
  - Safety
  - Effectiveness
  - Adjuvants
- DoD is purchasing 2.7M doses of unadjuvanted vaccine and 2.7 M doses of adjuvant

H1N1 vaccine – Where does DoD fit in?

- DoD will have it's own stockpile of H1N1 vaccine adequate to fully immunize 1.35M personnel
  - First use of this supply is to continue mission
  - May be used for AD, Activated Reservist, Title 10 NG, DoD civilians
  - Will also be used for OCONUS beneficiaries
  - Distribution is controlled by DoD
  - DoD will also receive supplemental vaccine for mission related activities

H1N1 vaccine – Where does DoD fit in?

- DoD also receives vaccine via the National Pandemic Vaccine Targeting and Allocation Guidelines
  - DoD receives vaccine directly from HHS for operational requirements – 1.5M people
  - DoD receives vaccines via local allocations to States for dependents, retirees and CONUS health care personnel
  - PHEO at each installation MUST work with local Public Health to make certain the installation is included in the State distribution plan

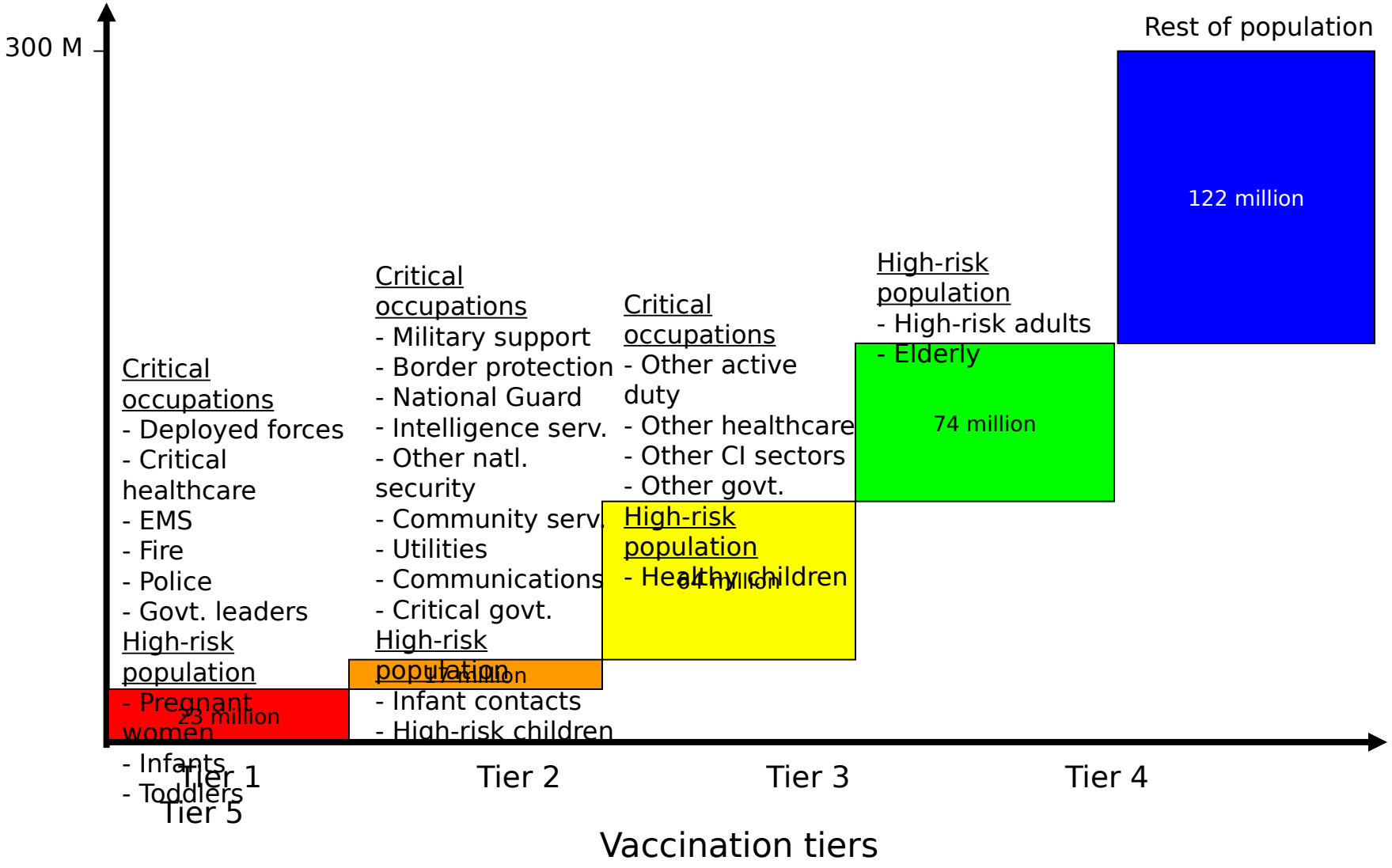
National Pandemic Vaccine Allocation Guidelines

4 groups to receive vaccine

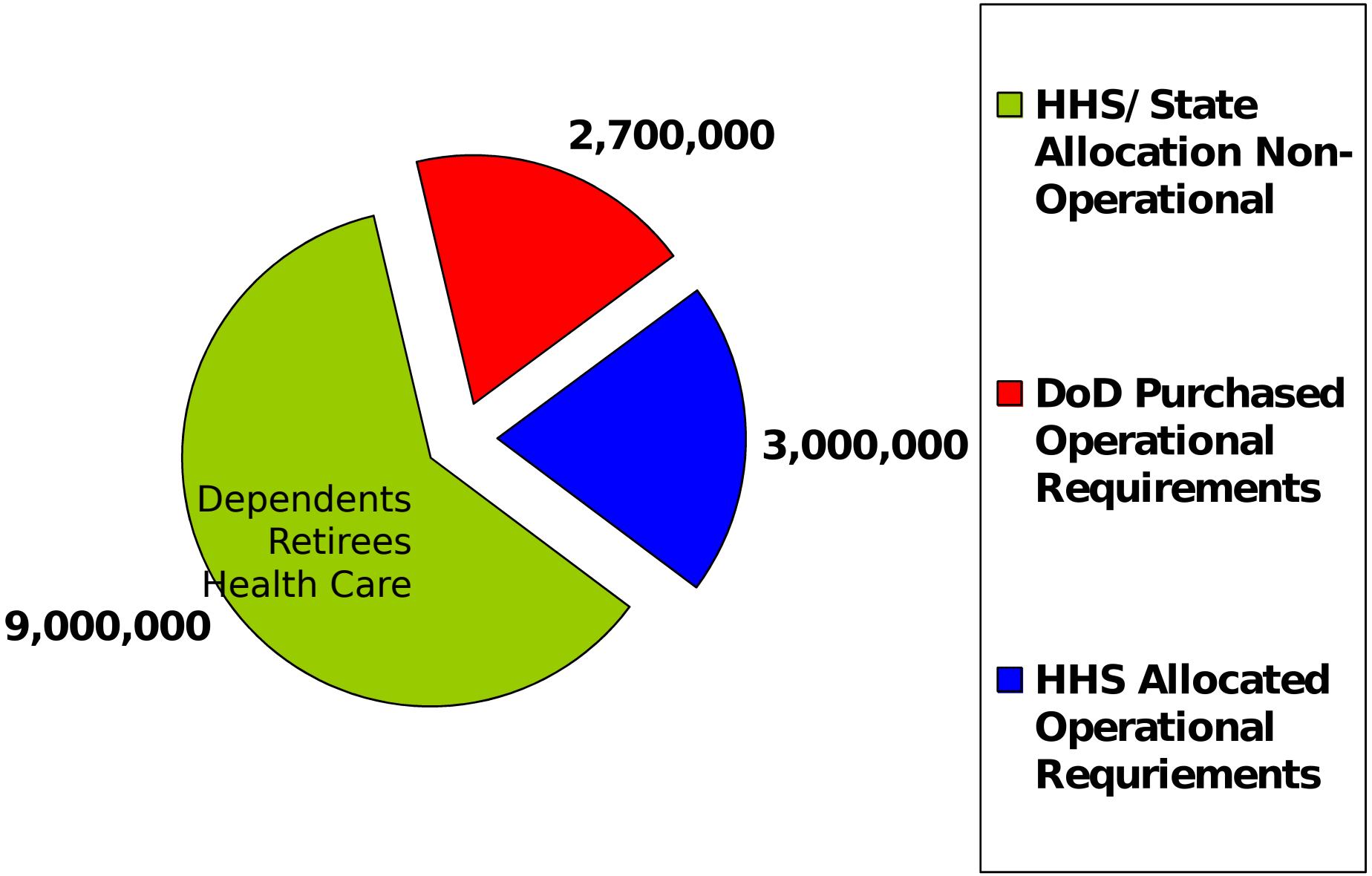
- National Defense
- Critical Infrastructure
- Health Care
- General population

- Each group divided into tiers
- Tiers filled simultaneously

Vaccination Tiers for Pandemic Vaccine



The Vaccine Pie, where DoD get's it's vaccine (doses)



DoD Draft Strategy

- Second wave with low morbidity/mortality
  - Target groups at highest risk of transmission
    - Training sites
    - Ships afloat
    - Deployed
- Second wave with high morbidity/mortality
  - Target groups with highest operational impact
    - Deployed
    - COOP
    - Essential personnel

Something to look forward to!

- Seasonal and H1N1 immunization programs will overlap
- H1N1 disease will probably appear before or at the same time the vaccine is available
- Mission related vaccine supply will be pushed out via DoD
- Vaccine for dependents and retirees will come from State supplies with points of distribution on the installation

Pandemic Flu Kits

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Project ID: 14723
Description: 14723_DoD_RC-690_Bag
Revision: 01
Date: 07.29.08
Source File: DoD_Bag_072908.ai

PREPARATION IS POWER

DoD Beneficiaries

Pandemic Flu Preparedness Kit

CONTENTS INCLUDE:

- Pandemic Information Sheet
- (2) N95 Respirators
- (4) Surgical Masks
- (1) Hand Sanitizer 4oz bottle

Front

YOU CAN MAKE A DIFFERENCE

By taking basic precautions you can protect yourself and your family from pandemic influenza. This kit includes instructions on how to decrease your risk of catching pandemic flu and what to do when someone in your family catches pandemic flu. Also included in this kit is a starter supply of waterless hand washing solution and two types of protective masks. The supplies in this kit will not be sufficient for the entire pandemic. You will be required to purchase replacement supplies as the pandemic proceeds. There is no influenza pandemic yet. Local health and government authorities will notify you when it is known that a pandemic is beginning and when it is in your community. This kit should be used when the pandemic arrives. The instruction guide inside this kit should be read now and kept with the kit for use when needed. These or similar kits might not be provided to the general public. We have provided these kits due to our commitment to the health of the DOD family as it directly impacts our ability to carry out the DOD mission.

WHERE CAN I GET MORE INFORMATION?

www.dod.mil/pandemicflu
www.pandemicflu.gov

Department of Defense | Force Health Protection and Readiness
5113 Leesburg Pike, Suite 901 | Falls Church, VA 22041
http://fhp.osd.mil

Back

PPE for the DoD Community

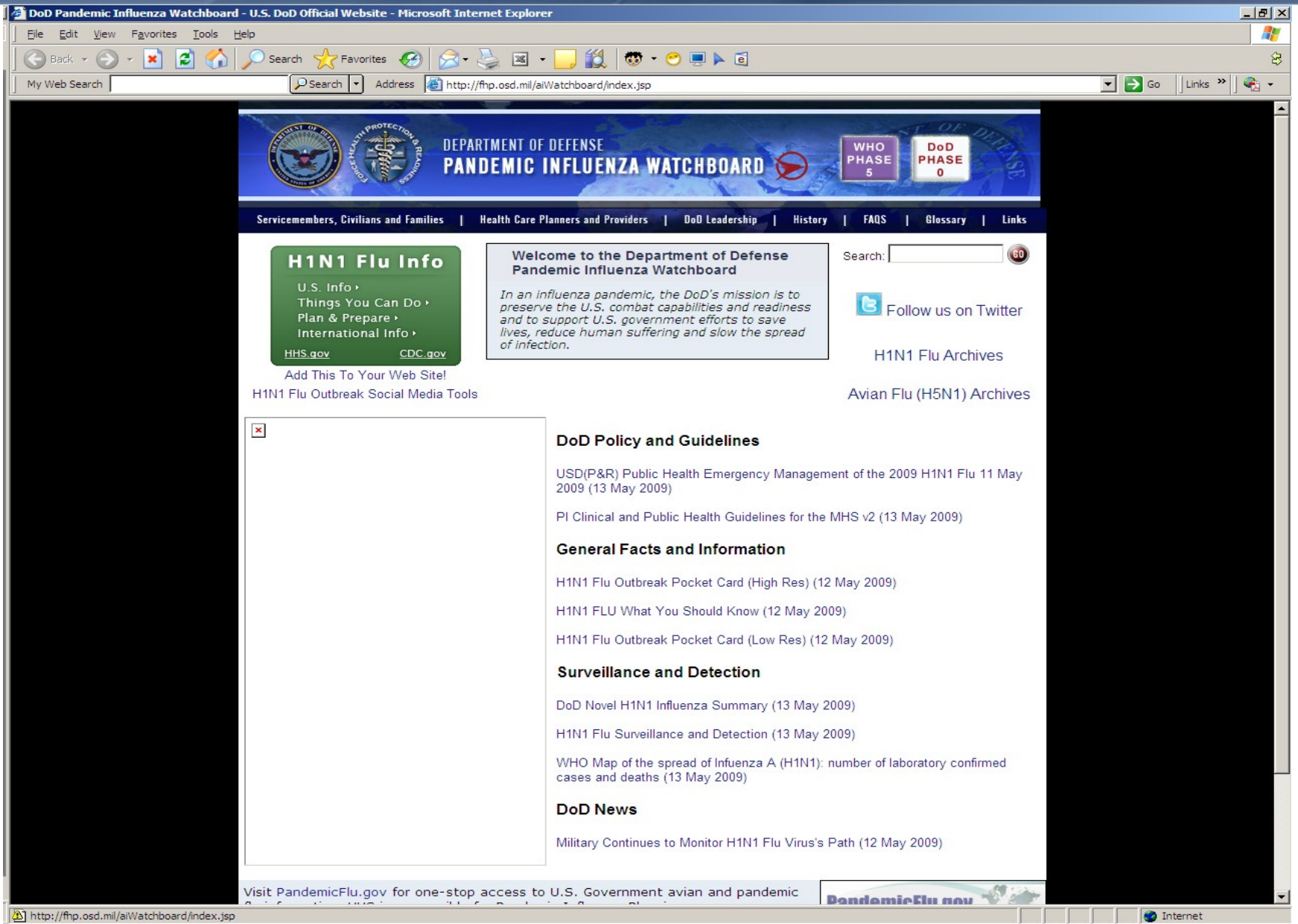
- Pandemic flu kits
  - Contains:
    - Personal risk mitigation instructions
      - Social distancing
      - Infection control
      - Mask instruction
    - Two N95 respirators
    - Four surgical masks
    - 4 oz. bottle of alcohol-based hand washing solution

Prioritizing Delivery of Medical Care During Pandemics and Other Public Health Emergencies of National Significance

- Establishes two primary objectives:
  - Support National Security Mission
  - Provide for TRICARE Prime and Plus enrolled beneficiaries
- MTF commanders must meet both objectives
- Minimum Standard of Care will equal that of the local community
- If plan is to transition care to non-DoD providers, must be done BEFORE the emergency and communicated to those impacted

- Standard of Care or access to medical resources will not be equal
  - Community baseline as minimum
  - Those who may have a lower medical risk may receive more resources due to operational requirements
- Need for transparency and communication with beneficiary population

www.dod.mil/pandemicflu


DoD Pandemic Influenza Watchboard - U.S. DoD Official Website - Microsoft Internet Explorer
http://fhp.osd.mil/aiWatchboard/index.jsp
DEPARTMENT OF DEFENSE
PANDEMIC INFLUENZA WATCHBOARD
WHO PHASE 5
DoD PHASE 0
Servicemembers, Civilians and Families | Health Care Planners and Providers | DoD Leadership | History | FAQS | Glossary | Links
H1N1 Flu Info
U.S. Info
Things You Can Do
Plan & Prepare
International Info
HHS.gov
CDC.gov
Add This To Your Web Site!
H1N1 Flu Outbreak Social Media Tools
Welcome to the Department of Defense Pandemic Influenza Watchboard
In an influenza pandemic, the DoD's mission is to preserve the U.S. combat capabilities and readiness and to support U.S. government efforts to save lives, reduce human suffering and slow the spread of infection.
Search:
GO
Follow us on Twitter
H1N1 Flu Archives
Avian Flu (H5N1) Archives
DoD Policy and Guidelines
USD(P&R) Public Health Emergency Management of the 2009 H1N1 Flu 11 May 2009 (13 May 2009)
PI Clinical and Public Health Guidelines for the MHS v2 (13 May 2009)
General Facts and Information
H1N1 Flu Outbreak Pocket Card (High Res) (12 May 2009)
H1N1 FLU What You Should Know (12 May 2009)
H1N1 Flu Outbreak Pocket Card (Low Res) (12 May 2009)
Surveillance and Detection
DoD Novel H1N1 Influenza Summary (13 May 2009)
H1N1 Flu Surveillance and Detection (13 May 2009)
WHO Map of the spread of Infuenza A (H1N1): number of laboratory confirmed cases and deaths (13 May 2009)
DoD News
Military Continues to Monitor H1N1 Flu Virus's Path (12 May 2009)
Visit PandemicFlu.gov for one-stop access to U.S. Government avian and pandemic
PandemicFlu.gov
http://fhp.osd.mil/aiWatchboard/index.jsp
Internet

Communication

- DoD sources
  - www.dod.mil/pandemicflu
    - Provides information for service members, DOD civilians, family members, health care planners and providers and DOD leadership
    - Includes links to other DOD and USG sites
- National sources
  - www.pandemicflu.gov
    - National website with links to HHS, CDC and other USG and international agencies
- International sources
  - http://www.who.int/csr/disease/avian_influenza/en/
    - WHO site includes guidance as well as current status
  - http://www.eiss.org/html/pandemic_europe.html
    - European Influenza Surveillance – includes guidance and plans by country

DoD Wish List

- Should funding be provided
  - Relenza
  - PPE
  - Pneumococcal vaccine
  - PI kits
  - More vaccine under direct DoD control

The fact is, compared to pigs, we humans are unforgivably slow to learn from pragmatic experience.

Karl Schwen

U.S. author. *In A Pig's Eye* (1985).

Questions?